PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference DK62328PC/mo	**FOR FURTHER ACTION**	See Form PCT/IPEA/416
International application No. PCT/EP2004/009170	International filing date *(day/month/year)* 16.08.2004	Priority date *(day/month/year)* 14.08.2003
International Patent Classification (IPC) or national classification and IPC C12N15/11, A61K31/711, G01N33/53		
Applicant DEUTSCHES KREBSFORSCHUNGSZENTRUM et al.		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 12 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. ☒ *sent to the applicant and to the International Bureau)* a total of 7 sheets, as follows:
      ☒ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

☒	Box No. I	Basis of the opinion
☐	Box No. II	Priority
☒	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☐	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☒	Box No. VI	Certain documents cited
☐	Box No. VII	Certain defects in the international application
☒	Box No. VIII	Certain observations on the international application

Date of submission of the demand	Date of completion of this report
11.08.2005	10.11.2005
Name and mailing address of the international preliminary examining authority: European Patent Office - P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Tx: 31 651 epo nl Fax: +31 70 340 - 3016	Authorized Officer Gruber, A Telephone No. +31 70 340-8997

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/EP2004/009170

Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:
   - ☐ international search (under Rules 12.3 and 23.1(b))
   - ☐ publication of the international application (under Rule 12.4)
   - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the **elements*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

Description, Pages

1-30 as originally filed

Sequence listings part of the description, Pages

1-4 as originally filed

Claims, Numbers

1-29 received on 11.08.2005 with letter of 11.08.2005

Drawings, Sheets

1/9-9/9 as originally filed

☒ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing

3. ☐ The amendments have resulted in the cancellation of:
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

* *If item 4 applies, some or all of these sheets may be marked "superseded."*

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 25-29 (all partially)

because:

☒ the said international application, or the said claims Nos. 25-29 (all with respect to industrial applicability) relate to the following subject matter which does not require an international preliminary examination (specify):

see separate sheet

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the said claims Nos.

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form	☐	has not been furnished
	☐	does not comply with the standard
the computer readable form	☐	has not been furnished
	☐	does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See separate sheet for further details

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	2-7,9-12,14,16-18,27-29
	No:	Claims	1,8,13,15,19-26
Inventive step (IS)	Yes:	Claims	7
	No:	Claims	1-6,8-29
Industrial applicability (IA)	Yes:	Claims	1-24
	No:	Claims	

2. Citations and explanations (Rule 70.7):

see separate sheet

Box No. VI Certain documents cited

1. Certain published documents (Rule 70.10)

and / or

2. Non-written disclosures (Rule 70.9)

see separate sheet

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

Supplemental Box relating to Sequence Listing

Continuation of Box I, item 2:

1. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this report has been established on the basis of:

   a. type of material:

   ☒ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material:

   ☒ in written format

   ☒ in computer readable form

   c. time of filing/furnishing:

   ☒ contained in the international application as filed

   ☒ filed together with the international application in computer readable form

   ☐ furnished subsequently to this Authority for the purposes of search and/or examination

   ☐ received by this Authority as an amendment on

2. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

3. Additional observations, if necessary:

The present application describes SGT (short for: small glutamine-rich tetratricopeptide repeat-containing protein)-specific siRNA, a SGT gene antisense molecule, a SGT mRNA specific ribozyme, an antibody against a SGT polypeptide, and a SGT-specific aptamer for inhibiting cancer.

Amendment

1 The amendments of the claims filed with the letter dated 11 August 2005 meet the requirements of Article 34(2)(b) PCT.

The following documents (D) are referred to in this communication; the numbering will be adhered to in the rest of the procedure:

D2: FONTE VIRGINIA ET AL: "Interaction of intracellular beta amyloid peptide with chaperone proteins." PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA. UNITED STATES 9 JUL 2002, vol. 99, no. 14, 9 July 2002, pages 9439-9444

D3: WO 01/77168 A (CORIXA CORPORATION; LODES, MICHAEL, J; WANG, TONGTONG; MOHAMATH, RAODO) 18 October 2001

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

Claims 25-29 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

2 The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of independent claims 1,8,13,15,19-26 is not new in the sense of Article 33(2) PCT.

The document D3 discloses (the references in parentheses applying to this document): a 349 aa long sequence (SEQ ID NO: 434; claim 2) in which aa 37-349 are 100% identical to the entire SEQ ID NO:1 of the present application. D3 further discloses antibody (claim 5), antisense oligonucleotides (page 45, last paragraph - page 46, first paragraph), ribozymes (page 47, paragraph 2), pharmaceutically-acceptable carriers (pages 73-74), screening method (page 56, paragraph 2) for lung cancer therapy and diagnosis (page 1, paragraph 1).

Note: Regarding the applicant's letter dated 11 August 2005, page 2, section 3.1: The expression "polypeptide having ... SEQ ID NO:1", in contrast to the expression "polypeptide consisting of ... SEQ ID NO:1", is not limiting and thus, comprises the sequence disclosed in D3.

However, even if the subject-matter of the respective claims would have been restricted to "polypeptide consisting of ... SEQ ID NO:1" , the degree of sequence identity between SEQ ID NO:1 of the present application and SEQ ID NO:434 of D3 is such that the antagonists of the present application are already embraced by the subject-matter disclosed in D3. Thus, the subject-matter of claims 1,8,13,15,19-26 would still not be new in the sense of Article 33(2) PCT.

Note: Regarding the applicant's letter dated 11 August 2005, page 2, section 4: D3 discloses that SGT is overexpressed in lung small cell carcinoma plus metastatic tissue (example 1; pages 101-102; table 2). Furthermore, D3 discloses the use of antisense constructs that inhibit abnormal cellular proliferation e.g. cancer (page 46, paragraph 1). Thus, the selection made

by the present application, i.e. the subject-matter relating to the inhibition of the propagation of an undesired cell population using SGT antagonists, is not novel (Art. 33(2) PCT) in the light of D3.
Furthermore, the latter selection does not have any unexpected property. Based on the teaching of document D3 it would be obvious for the skilled person to test whether an SGT antagonist, for example antisense molecules, are able to inhibit the growth of lung small cell carcinoma using routine experiments, such as merely conventional trial-and-error experimentation without employing skills beyond common general knowledge, and thus with skills that lack inventive step (Article 33(3) PCT).

3 Claims 2-7,9-12,14,16-18,27-29 formally meet the requirements of Article 33(2) PCT because their subject-matter was not disclosed in the available prior art.

4 In the light of document D3 dependent claims 2-5,9-11,14,16-18,27,29 do not contain any features which, in combination with the features of any claim to which they refer, meet the requirements of the PCT because they are either not novel (Article 33(2) PCT) and/or they are merely one of several straightforward possibilities from which the skilled person would select, in accordance with circumstances, without the exercise of inventive skill (Article 33(3) PCT), in order to solve the problem posed.

5 The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claims 6,12,28 does not involve an inventive step in the sense of Article 33(3) PCT.

The closest prior art to the subject-matter of claims 6,12,28 is document D3, which makes the disclosure as stated above.

The difference, in terms of the claimed technical features, between the claimed invention on the one hand and the closest prior art document D3 on the other is the use of SGT-specific siRNA.

The technical effect caused by this technical difference is not different from the effect caused by the antagonists described in the closest prior art document D3.

Therefore, the objective technical problem underlying the claimed invention is the provision of alternative SGT antagonists.

The solution proposed in the present application is the use SGT-specific siRNA.

Document D2 describes the double-stranded RNA inhibition of a SGT ortholog (abstract, lines 18 - 21; page 9440, left column 3rd paragraph - page 9440, right column, 1st paragraph; page 9442, right column, 2nd paragraph - page 9443, left column, 1st paragraph).
In view of the teaching of document D2, it would be obvious to the person skilled in the art, namely when the same result is to be achieved, to apply these features with corresponding effect to a process according to document D3, thereby arriving at SGT-specific siRNA according to claims 6,12,28.

The subject-matter of claims 6,12,28 does therefore not involve an inventive step (Article 33(3) PCT).

6 The present application meets the criteria of Article 33(1) PCT, because the subject-matter of claim 7 involves an inventive step in the sense of Article 33(3) PCT.

The closest prior art to the subject-matter of claim 7 is document D3, which makes the disclosure as stated above.

The difference, in terms of the claimed technical features, between the claimed invention on the one hand and the closest prior art document D3 on the other is the use of SGT-specific siRNA defined by SEQ ID NO:3 and/or SEQ ID NO:4.

Therefore, the objective technical problem underlying the claimed invention is the provision of alternative SGT antagonists.

The solution proposed in the present application is the use SGT-specific siRNA defined by SEQ ID NO:3 and/or SEQ ID NO:4.

Document D2 describes the double-stranded RNA inhibition of a SGT ortholog (abstract, lines 18 - 21; page 9440, left column 3rd paragraph - page 9440, right column, 1st paragraph; page 9442, right column, 2nd paragraph - page 9443, left column, 1st paragraph).

However, neither D3 nor D2 suggest the use SGT-specific siRNA defined by SEQ ID NO:3 and/or SEQ ID NO:4

The subject-matter of claim 7 does therefore involve an inventive step (Article 33(3) PCT).

7 The subject-matter of claims 1-24 is susceptible of industrial application (Article 33(4) PCT).

8 For the assessment of the present claims 25-29 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

Re Item VI

Certain documents cited

Certain published documents

Application No Patent No	Publication date *(day/month/year)*	Filing date *(day/month/year)*	Priority date *(day/month/year)*
WO2004030615	15 April 2004	29 Sept. 2003	02 Oct. 2002

Re Item VIII

Certain observations on the international application

9 In order to avoid any ambiguity with regard to Rule 9.1(I) PCT, it should have been stated that the subject-matter of claims 15-18,23 is not performed on humans.

10 Present claims 1,5, 8,13,19-22,24-26,29 relate to compounds defined by reference to a desirable characteristic or property, namely by being an "antagonist of SGT" (claims 1,8,13,19-22,24-26,29), and a "transcriptional regulator of the SGT gene", "SGT-specific mutein" (both in claim 5) and "SGT-specific aptamer" (claims 5,20-22). The claims cover all compounds having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for only a very limited number of such compounds, i.e.:
SGT (short for: small glutamine-rich tetratricopeptide repeat-containing protein)-specific siRNA, a SGT gene antisense molecule, a SGT mRNA specific ribozyme, and an antibody against a SGT polypeptide, as mentioned in claim 5.

Therefore, the subject-matter of claims 1,5, 8,13,19-22,24-26,29 does not meet the requirements of Articles 5 and 6 PCT because the subject-matter is not sufficiently disclosed and supported.

Note: The view of the applicant (letter dated 11 August 2005, page 2, section 2) is not shared. The passage cited by the applicant (page 10, lines 6-10 of the present application) merely mentions the functional features that are common to aptamers, however it does not describe the specific functional features that the aptamer must have in order to be a hSGT antagonist. Furthermore, the sequence of for example a SGT-specific ribozyme can be directly deduced from the sequence of SGT, while the sequence of for example an aptamer or a transcriptional regulator cannot. The same applies to the other terms mentioned above.

11 Claims 8,13,26 define the disease to be treated with an antagonist of SGT as a disease which is caused by the propagation of an undesired cell population. The functional terms used to define the disease to be treated are acceptable as long as the claim still meets the requirements of Article 6 PCT. The requirement of clarity demands not only that the skilled person be able to understand the wording of the

claim but also that he be able to implement it. In other words, the functional feature must be accompanied by instructions which are sufficiently clear for the expert to reduce them to practice. This implementation of the invention implies that means must be available to the skilled person, either from the patent application or from the common general knowledge at the relevant date of the application, to recognise and evaluate the technical effect of the functional definition.
When the claim is directed, according to the usual wording, to a further therapeutic application of a medicament and the condition to be treated is defined in functional terms, such as those in the claims 8,13,26, the skilled person must be given instructions, in the form of experimental tests or any testable criteria, allowing him to recognise which disease falls within the functional definition and accordingly whether or not the therapeutic indication representing the heart of the invention falls within the scope of the claim.
As a consequence, claims 8,13,26 lack clarity in the sense of Article 6 PCT.

Note: The view of the applicant (letter dated 11 August 2005, page 2, section 2) is not shared. The description "disease which is caused by the propagation of an undesired cell population" comprises diseases such as cancer but also for example bacterial diseases. Furthermore, even if restricted to for example cancer it is dubious that any cancer can be treated with a hSGT antagonist.

12 Claim 19 refers back to the method of claim 14. However, this is a contradiction since claim 14 relates to a compound while claim 19 relates to a method.